

REMARKS

Status of the Claims

Claims 1-10 and 15-21 were pending.

Claims 1-10 and 15-21 have been rejected under 35 U.S.C. 112, first and second paragraphs.

Claims 5 and 17-19 are canceled in this amendment.

New Claim 22 has been added.

Amendment of the Specification and New Claim

The Specification has been amended to correct certain typographical errors that appear in paragraphs (i) and (ii) of the definition of T¹-T⁹. Basis for the amendments are discussed below in the "Rejections under 35 U.S.C. 112, second paragraph" section under the second point. Also, new Claim 22 has been added. Basis can be found in original claims 6, 7 and 8.

Applicants believe that the present amendments made to the Specification and Claims do not add new matter, nor do they broaden the scope of what is claimed.

Rejections under 35 U.S.C. 112, first paragraph

Claims 1-10 and 15-21 have been rejected under 35 U.S.C. 112, first paragraph as the Examiner contends that the scope of "prodrug" is not enabled. Applicants disagree, as it is believed that one of skill in the art of medicinal chemistry could combine the teachings of the present specification with what is known in the art about prodrugs to make and use prodrugs of the present invention. (*See e.g.* Greene, Theodora W., et al., Protective Groups in Organic Synthesis, 3rd ed. referred to in the Specification, page 44, lines 10 and 11). However, to expedite issuance of the present case, the term "prodrug" has been deleted throughout the claims.

Also, claims 15-19 have been rejected under 35 U.S.C. 112, first paragraph as being non-enabling. The Examiner only addresses claim 19, contending that the scope of the method-of-use is not enabled simply based on inhibition of leukocyte activation. The Examiner further contends that no screening protocols are described, and that no working examples on the use of "dihydropyrimido[5,4-b][1,4]oxazines and 7,8-dihydro-6H-pyrimido[5,4-b][1,4]thiazines have been presented. Applicants disagree. The art cited extensively throughout the background identifies leukocyte active compounds as being useful in the treatment of the leukocyte-activated disorders. Moreover, screening protocols are described on pages 50 and 51 of the specification. However, claim 19 has been canceled in order to expedite prosecution of the present case.

The Examiner did not detail a reason for the enablement rejection of claims 15-18. This rejection is moot, however, with respect to claims 17 and 18 as they have been canceled. However, Applicants have added “a pharmaceutically acceptable excipient or diluent” to composition claims 15 and 16. Basis for this amendment and examples of such compositions can be found on pages 17-19 of the specification.

Applicants reserve the right to file a continuing application on the canceled subject matter discussed above and other unclaimed subject matter of the application. Applicants believe all the rejections under 35 U.S.C. 112, first paragraph have been addressed or rendered moot and respectfully request withdrawal of the claims for lack of enablement.

Rejections under 35 U.S.C. 112, second paragraph

Applicants appreciate the Examiner’s careful review of the present application. The Examiner has rejected claims 1-10 and 15-21 under 35 U.S.C. 112, second paragraph for a number of reasons which are either traversed or addressed below.

First, under number 4, on pages 5-8 of the Office Action the Examiner contended that the claims were indefinite under letters a), b), c), e), f), r), s), t) u), v), w), and x) for not specifying the point of attachment of certain moieties. The claims have been amended to specify the point of attachment of said moieties according to their appropriate valency in the definition of T¹-T⁹ in paragraphs (i) and (ii) of independent claims 1 and 6.

Secondly, under number 4, letters d), g), t), and w) the Examiner observes that the moiety “-T¹²N(T¹⁶)-T¹⁵-T¹⁰” is vague and indefinite in the claims as T¹⁵ is inappropriately assigned to be a divalent moiety. This is a typographical error which has been corrected in the moiety (to -T¹²N(T¹⁶)-T¹³-T¹⁰) in the Specification and independent claims 1 and 6 under the definition of T¹-T⁹ in paragraphs (i) and (ii).

Thirdly, under letter h) the third moiety in line 3 of claim 3 recites the possibility of 0-4 substituents. Applicants have amended claim 3 to recite the maximum number of substituents available on this moiety as recited in independent claim 1 (i.e. 0-2).

Fourth, under letter i), the Examiner contends there is insufficient antecedent basis in the claim 3 definition of Y⁵ for the limitation “haloalkyl”. In response, Applicants have deleted the limitation “haloalkyl” from the definition of Y⁵ in claim 3.

Fifth, since the rejections detailed by the Examiner in letters j) through p) all pertain to claim 5, which has been canceled, these rejections are all moot.

Sixth, under letter y), the Examiner contends that in claim 7 there is insufficient antecedent basis for the limitation “-NH-CH₂CH₂NHC(=O)CH₃ in the definition of Z. Applicants traverse. Z is -NR³R⁴ where R³ can be H and R⁴ can be alkyl substituted by T⁴ (which can be ethyl substituted by “-T¹²N(T¹⁶)-T¹³-T¹⁰”, or “-NHC(O)CH₃” (see second point, above).

Seventh, under letter z), the Examiner contends that in claim 8 there is insufficient antecedent basis for the limitation “3-CH₃C(=O)NHpyrrolidin-1-yl” in the definition of Z. Applicants traverse. Z is -NR³R⁴ where R³ and R⁴ are taken together to form a heterocyclo (pyrrolidinyl) which can be substituted by T⁴ which can be “-T¹²N(T¹⁶)-T¹³-T¹⁰”, or “-NHC(O)CH₃” (see second point, above).

Eighth, under letters aa), ab), ac), ad) and ae), it is presumed that the Examiner contends that moieties in the definition of R₅ (not Z) of claim 8 containing a limitation that may be summarized as “4-(alkyl)SO₂NHbenzyl” lacks insufficient antecedent basis. Applicants traverse. According to the definition, R₅ can be an (aryl)alkyl (i.e. benzyl) that can be substituted by T⁷ which can be “-T¹²N(T¹⁶)-T¹³-T¹⁰”, or “-NHSO₂(alkyl)” (see second point, above).

Ninth, under letters af) and ag) the Examiner rejected claim 16 noting that claim 21 is not a composition claim and that it was also dependent upon a canceled claim. The Examiner also objected to claim 16 contending that it was an improper multiple dependent claim. In response, Applicants have amended the claim to recite the appropriate dependency and incorporated the substance of claim 21.

Tenth, under the letters ah) and ai), the Examiner rejected claims 17 and 18 contending that they were substantial duplicates of claim 15 and that the therapeutic agent in said claims was described in “relative terms” and was therefore indefinite. Further, under letter (aj) the Examiner contended that alleged “methods of use” in claim 17 and 19 were also indefinite according to a Wands factor analysis as allegedly there was not enough information in the specification to enable one of skill in the art to practice the claimed use of the compounds of the present invention. Applicants disagree as the Utility section of the specification is replete with definitions of said terms in claim 17 and 18. Moreover, given the extensive art cited in the Background, one of skill could combine what is known in the art about patent response, dosing regimens etc. in combination with the information about the present invention given in the specification to practice the method of claim

19 without undue experimentation. However, in order to expedite the issuance of this application claims 17-19 have been canceled and claim 20 re-written in independent form. Also, claim 21 has been written in independent form. Applicants reserve the right to file continuing applications on these canceled claims and other unclaimed subject matter.

In summary, Applicants believe all the rejections of the claims under 35 USC 112, first and second paragraphs, have been either addressed or rendered moot. Applicants respectfully request withdrawal of the enablement and indefiniteness rejections and believe the claims are now in condition for allowance.


FEES

One new independent claim has been added and one has been canceled. Also, two claims were re-written into independent form, but four dependent claims have been canceled. If it is determined that a fee is due, please charge same to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

The Examiner is invited to contact the undersigned by telephone, at the number listed below, if it is believed that a telephonic communication would facilitate the prosecution of this application.

Respectfully submitted,

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